EXHIBIT 27

PocketGuide

Pain with Appropriate Use of Opioids

2010

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Assessment

Management With Opioids

Selecting a Treatment Regimen

AMERICAN SOCIETY OF PAIN EDUCATORS

International Guidelines Center

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Table 1. Pain Assessment

Checklist

- **History — past, social and family history**
- **Physical examination**
- **Pain**
  - Location (may be multiple)
  - Category (see Table 2)
  - Intensity (see Table 3)
  - Course: onset, duration, fluctuation, rhythms, aggravating/alleviating factors
  - Etiology: primary disease/condition, therapy/procedure, comorbidities
- **Effects of pain on patient**
  - Impaired functioning (physical, mental), quality of life
  - Accompanying symptoms (eg, nausea, impaired sleep, loss of appetite, decreased activity)
  - Emotional distress (eg, crying, angry, anxious, depressed, suicidal)
  - Impaired relationships (eg, family, school, occupational, social)
- **Special issues**
  - Psychiatric or substance abuse history
  - Patient/family/significant others' knowledge and beliefs about pain
  - Communication barriers; minority/cultural factors
  - Litigation or worker's compensation
  - Screening tests for risk of substance abuse
- **Special populations (eg, pediatric, geriatric, pregnancy/lactation, substance abuse/addiction, cognitive impairment)**
- **Relevant laboratory and imaging studies based on data from patient history and examination**

Management

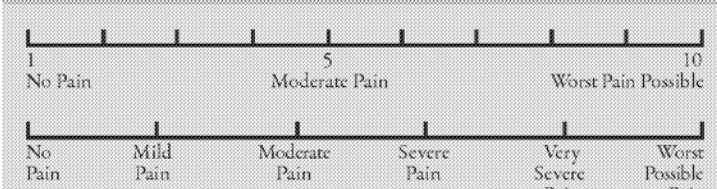
- **Reassess at specified intervals and with same pain scale to evaluate intended effect of therapy.**
- **Therapeutic goal is satisfactory pain control (usually below 4 on a scale of 10) with tolerable side effects and acceptable quality of life (physical, psychological, occupational, social functioning).**
- **Critical to distinguish tolerance, dependence, and pseudoaddiction from addiction (see Table 7).**

Table 2. Categories of Pain*

- **Acute (eudynia): usually related to an identifiable trauma or medical condition; subsides within days or weeks as condition resolves.**
- **Chronic (maldynia): may/may not be related to identifiable pathology; may persist indefinitely; frequently associated with mood disturbances, physical dysfunction, social disruption.**
- **Neuropathic: acute or chronic pain resulting from peripheral or central nervous system pathology; described as sharp, shooting, tingling and/or burning, electric; often associated with neurological deficits.**
- **Nociceptive: acute or chronic pain related to tissue damage, involving direct stimulation of intact nociceptors, and relayed along normally functioning nerves.**
- **Somatic (from skin, soft tissue, muscle, bone): sharp/stabbing, aching and/or throbbing pain — easily localized.**
- **Visceral (from internal organs): gnawing, cramping, deep and/or pressing pain difficult to describe and localize; may be concurrent nausea, vomiting or diarrhea.**

*In documentation, use patient's own words to describe pain.
Adapted from: Emanual LL, von Gunten CF, Ferris FD. The Education for Physicians on End-of-Life Care (EPEC) curriculum. Module 4, Pain Management. EPEC Participant's Handbook. EPEC Project. Princeton, NJ: The Robert Wood Johnson Foundation; 1999.

Table 3. 1-10 Numeric Pain Rating and Intensity Scale



From: Acute Pain Management: Operative or Medical Procedures and Trauma, Clinical Practice Guideline No. 1, AHCPR Publication No. 92-0032; February 1992. Agency for Healthcare Research & Quality. Rockville, MD; pages 116-117.
NO PAIN
MILD PAIN (you know it's there but hardly notice it)
MODERATE PAIN (a little more pain than mild pain – it does not stop you from doing things)
SEVERE PAIN (wakes you from sleep or makes you stop your activity to ease the pain)
VERY SEVERE PAIN (you cannot stand the pain and are unable to do any activity or sleep)
WORST POSSIBLE PAIN (the worst pain you can imagine)

Table 4. Addiction Assessment Tools

SOAPP®-R

0 = Never 1 = Seldom 2 = Sometimes 3 = Often 4 = Very Often

To score the SOAPP, add the ratings of all the questions. A score of 18 or higher is considered positive.

HOW OFTEN:	0 1 2 3 4
1. Do you have mood swings?	
2. Have you felt a need for higher doses of medication to treat your pain?	
3. Have you felt impatient with your doctors?	
4. Have you felt that things are just too overwhelming that you can't handle them?	
5. Is there tension in the home?	
6. Have you counted pain pills to see how many are remaining?	
7. Have you been concerned that people will judge you for taking pain medication?	
8. Do you feel bored?	
9. Have you taken more pain medication than you were supposed to?	
10. Have you worried about being left alone?	
11. Have you felt a craving for medication?	
12. Have others expressed concern over your use of medication?	
13. Have any of your close friends had a problem with alcohol or drugs?	
14. Have others told you that you had a bad temper?	
15. Have you felt consumed by the need to get pain medication?	
16. Have you run out of pain medication early?	
17. Have others kept you from getting what you deserve?	
18. In your lifetime, have you had legal problems or been arrested?	
19. Have you attended an AA or NA meeting?	
20. Have you been in an argument that was so out of control that someone got hurt?	
21. Have you been sexually abused?	
22. Have others suggested that you have a drug or alcohol problem?	
23. Have you had to borrow pain medications from your family or friends?	
24. Have you been treated for an alcohol or drug problem?	
TOTAL SCORE	

Sum of Questions	SOAPP®-R Indication
≥ 18	+
< 18	–

Screening Instrument for Substance Abuse Potential (SISAP)
For predicting addiction risk in patients receiving opioids.
Access at: http://www.wehealny.org/stoppain/ped/_pdf/opioidchapter9.pdf

Drug Abuse Screening Tool (DAST-20)
For detecting potential drug abuse or dependency disorders in patients.
Access at: http://adai.washington.edu/instruments/pdf/Drug_Abuse_Screening_Test_105.pdf

Opioid Risk Tool (ORT)
For predicting patients at high and low risk for opioid-related aberrant behavior.
Access at: http://www.lifetreeresearch.com/media/articles/ORT.pdf

Cage Adapted to Include Drugs (CAGE-AID)
For detecting potential drug abuse or dependency disorders in patients.
Access at: http://www.mqic.org/pdf/CAGE_CAGE_AID_QUESTIONNAIRES.pdf

ORT

		Female	Male
1. Family history of substance abuse	Alcohol Illegal drugs Other	[ ] 1 [ ] 2 [ ] 4	[ ] 3 [ ] 3 [ ] 4
2. Personal history of substance abuse	Alcohol Illegal drugs Other	[ ] 3 [ ] 4 [ ] 5	[ ] 3 [ ] 4 [ ] 5
3. Age (if between 16 - 45)		[ ] 1	[ ] 1
4. History of Preadolescent Sexual Abuse		[ ] 3	[ ] 0
5. Psychological Disease	ADD, OCD, Bipolar, Schizophrenia Depression	[ ] 2 [ ] 1	[ ] 2 [ ] 1
Low (0-3) Moderate (4-7) High (8+)	Total	[ ]	[ ]

Source: Webster LR, Webster RM, Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the Opioid Risk Tool. Pain Med 2005; 6(6):432-442.
Adapted from: Cross Validation of a Screener to Predict Opioid Misuse Among Chronic Pain Patients (SOAPP-R). Inflexxion, Inc. http://www.painedu.org/soapp-development.asp.

Figure 1. Assessment and Treatment for Chronic Pain

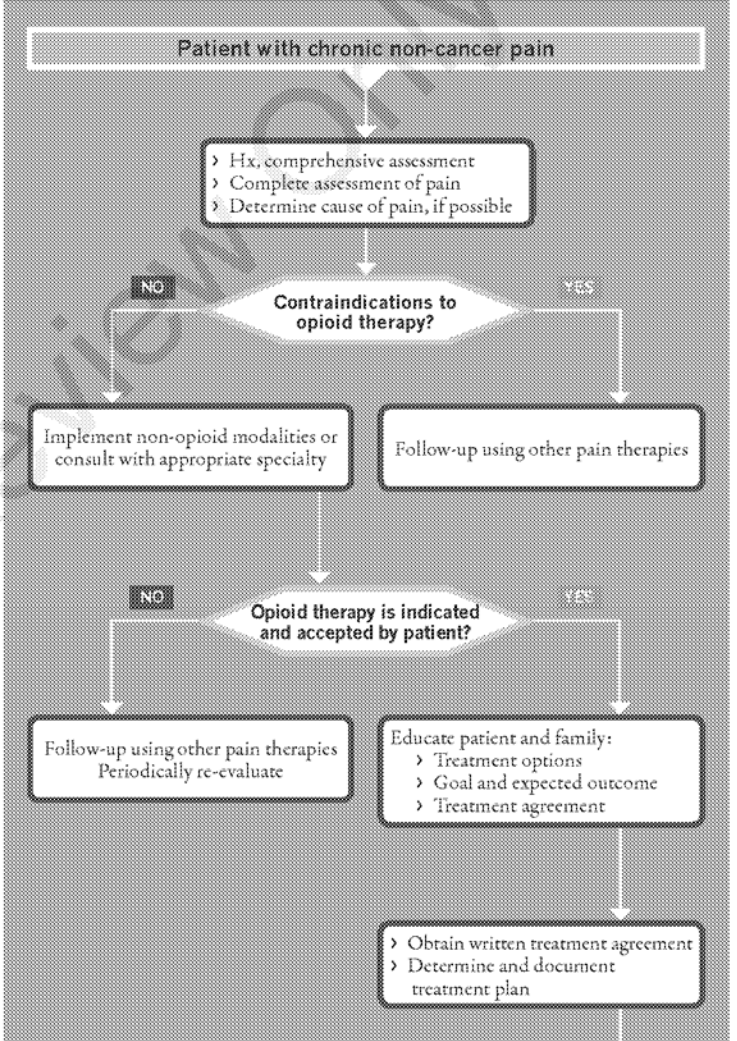


Table 5. Principles of Pain Management with Opioids

Acute pain (eudynia)

- → Establish diagnosis and treat underlying conditions
- → Determine associated pain location, intensity, and category (see Tables 1, 2, 3)
- → Symptomatic treatment of acute pain should be multimodal, with possible application of:
  - › Non-pharmacologic approaches (eg, heat, ice, rest, massage, education)
  - › Non-opioids (eg, ASA, APAP, NSAIDs, COXIBs)
  - › Opioids titrated to effect (see Table 8)
- → Use least invasive route of administration
- → Treat pain before it becomes severe; dose PRN
- → Risk of addiction is low (see Table 7)

Chronic non-cancer pain (maldynia)

- → Establish diagnosis and treat underlying conditions
- → Patients may be considered for therapeutic trial of opioids
- → Complex patients (eg, addiction, medical problems, psychopathology, rehabilitation issues) may need management in specialty setting
- → Written treatment plan (individualized to patient and pain problem) includes:
  - › Medication(s) (name, dose, frequency)
  - › Measurable objectives (clinical outcomes)
  - › Informed consent (risks/benefits of opioid therapy)
  - › Physician-patient therapeutic agreement (terms/conditions for prescribing opioids)
- → Prepare exit strategy for patients failing to meet specific goals of agreed-on therapy

Cancer-related pain

- → Establish diagnosis and treat underlying conditions
- → Pain prevention easier than relieving established pain — for constant chronic pain, dose ATC and use PRN doses for breakthrough pain
- → Appropriate opioid dose can relieve pain throughout dosing interval without unmanageable side effects
- → Single-entity opioids have no maximum dose but may be limited by side effects
- → Anticipate opioid-induced side effects and assess need for prophylactic medication (see Table 6)

Continued on next page.

Table 5. Principles of Pain Management with Opioids—*continued*

Rescue dose for breakthrough pain

- → Use same drug as standing drug. If not possible, use equianalgesic dose of same class of drug (see Tables 11a-c)
- → Step One: calculate total daily dose of opioid = ATC total (mg) + PRN total (mg) during 24-hour period
- → Step Two: use 10–15% of total daily dosage PO q 1-2 h PRN

If increase in long-acting regimen is required (pain remains uncontrolled)

- → If mild-moderate pain persists: increase total daily dose by 25-50%
- → If moderate-severe pain persists: increase total daily dose by 50-100%
- → Remember to adjust rescue dose to represent 10-15% of new total daily dose

If dose reduction is required (decreasing pain level and/or intolerable side effects)

- → If treated for several weeks with opioids, gradual reduction is indicated to prevent withdrawal symptoms
- → Symptoms include: yawning, sweating, lacrimation, rhinorrhea, anxiety, insomnia, dilated pupils, piloerection, tachycardia, hypertension, nausea/vomiting, cramping abdominal pains, diarrhea, and muscle aches and pains
- → Dose reductions should be no more than 10% per day
- → Alternative method: reduce dose by 50%, then reduce by 25 % every other day*
- → May stop completely when equivalent of 30 mg oral morphine daily is given for 2 days
- → Educate patients on difference between withdrawal and addiction, and provide plan of action for withdrawal symptoms

ALL PATIENTS

- → Periodic review
  - › Pain rating (intensity, category, location)
  - › Treatment effectiveness (goal established on 0 – 10 pain intensity scale)
  - › Patient's functional changes
  - › Side effects/adverse effects
  - › Patient adherence to regimen
- → Diligently documented medical records include:
  - › Patient visits
  - › Specialty consults
  - › Therapeutic/diagnostic procedures, lab results
  - › Prescriptions (eg, date, drug, strength, dosage units, route of administration, frequency)
  - › Document the 4 As (Analgesia, Activity, Adverse Side Effects, and Aberrant Behavior)**

*This is not based upon evidence-based guidelines

**Passik SD, Weinreb H.J. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. *Adv Ther.* 2000;17:70-83. Passik SD, Kirsh KL, Whitcomb L, et al. Pain clinicians' rankings of aberrant drug-taking behaviors. *J Pain Palliat Care Pharmacother.* 2002;16:39-49.

Adapted from: *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain.* Euless, TX: Federation of State Medical Boards of the United States, Inc.; 1998. *Pocket Guide for Pain Management in Adults.* Boston, MA: Tufts New England Medical Center; 1998. Scott CJ, Griffin CB, eds. *Pain Management Tables and Guidelines: Pain and Symptom Management.* Boston, MA: Brigham and Women's Hospital; 2000.

Table 6. Management of Opioid Side Effects

Confusion/delirium

- Assess for other causes (eg, other psychoactive agents, CNS pathology); check electrolytes, calcium, glucose
- Consider metabolic accumulation
- Consider adding non-opioid analgesic or consult specialist for interventional technique to achieve opioid dose reduction (see Table 9)
- Consider changing opioid (see Table 10)
- Consider neuroleptic agent (eg, olanzapine, risperidone)

Constipation (begin bowel regimen at onset of opioid therapy; goal is frequency/quality of movement acceptable to patient; tolerance does not develop)

- Increase fluids; exercise (when appropriate)
- Initiate stimulant laxative* (eg, senna, casanthranol) + stool softener (docusate) taken at fixed daily dose; consider increasing laxative dose when increasing opioid dose (opioid constipation is dose dependent)
- Consider adding non-opioid analgesic to allow opioid dose reduction
- Rectal examination to check for impaction; if found, disimpact
- Consider adding another agent (eg, magnesium hydroxide, bisacodyl, rectal suppository, lactulose, sorbitol, magnesium citrate; Fleet, saline, or water enema) when needed
- Consider prokinetic agent (eg, metoclopromide)
- Consider appropriateness of peripheral opioid receptor antagonists (eg, methylnatrexone)

Nausea/vomiting (prescribe antiemetics with initial opioid prescription; tolerance may develop)

- Assess for other causes (eg, constipation/obstruction, CNS pathology, chemotherapy, radiation therapy)
- Antiemetic ATC for few days to 1 week, then PRN (eg, prochlorperazine, thiethylperazine, metoclopromide, droperidol, ondansetron, haloperidol)
- Consider adding non-opioid medication to achieve opioid dose reduction
- Consider changing opioid or route of administration

Pruritis

- Consider antihistamine (eg, diphenhydramine, cetirizine, fexofenadine, doxepin)
- Consider switching opioids

Respiratory depression, hypoventilation (tolerance develops with chronic use)

- If respiratory depression suspected, FIRST assess for change in level of consciousness (attempt to arouse). Use caution when deciding to administer naloxone. Patients dependent on opioids may experience withdrawal with return of pain if given inappropriately.
  - > Review goals of care: naloxone is not indicated in dying patients as active dying process may cause changes in respiratory rate and arousal.
  - > If arousable: monitor patient closely, may not be appropriate for naloxone administration—reassess opioid dosing.
  - > If respiratory rate <8 AND there are data to support decreased ventilation (eg, low oxygen saturation, hypotension)—consider low-dose naloxone administration — this low-dose should help prevent withdrawal symptoms when reversing suspected overdose. Assess opioid regimen—may require naloxone infusion (or repeated doses) if long-acting agent contributed to overdose. [Dilute 1 amp (0.4 mg of naloxone) in a 10 mL syringe with 9 mL of saline. Then push at 1 mL per min (0.04 mg/mL).]

Sedation (tolerance often develops with chronic use)

- Assess degree of sedation, and as appropriate:
  - > Assess for other causes (eg, other psychoactive agents, hypercalcemia, CNS pathology, metastases, sepsis)
  - > Consider addition of caffeine, methylphenidate, dextroamphetamine, modafinil
  - > Consider titrating opioid dose downward to reduce sedation (if pain control can be maintained)
  - > Consider non-opioid analgesic to achieve opioid dose reduction
  - > Consider lower opioid dose administered – consistent with duration of action – could drive prescribing *q8h*
  - > Consider changing opioid

*If long-term use anticipated, use cautiously because of possibility of dependence.

Adapted from: *Use of Opioid Analgesics for the Treatment of Chronic Noncancer Pain–A Consensus Statement and Guidelines*. Canadian Pain Society; 1998. Cherny N, Ripamonti C, Pereira J, et al for the Expert Working Group of the European Association of Palliative Care Network. Strategies to manage the adverse effects of oral morphine: an evidence-based report. *J Clin Oncol* 2001;19:2542–2554. McNicol E, Horowicz-Mehler N, Fisk RA, et al. Management of opioid side effects in cancer-related and chronic noncancer pain–a systematic review. *J Pain* 2003;4:231–256.

Table 7. Analgesic Tolerance, Dependence, Addiction

Term	Definition	Comments
Tolerance	Neuroadaptation to effects of chronically administered opioids, requiring increasing doses to maintain analgesia or decreasing analgesia over time.	• *Not in itself* predictive/diagnostic of addiction • Treatment not required if dose stabilizes • Treatment includes changing opioids or adding non-opioid analgesic modalities • Dosages must be increased to produce the same effect
Physical dependence	Physiologic state in which abrupt cessation of opioid, or administration of opioid antagonist, results in withdrawal syndrome: eg, agitation, tachycardia, hypertension, piloerection, coryza, tremors, sweats, chills, lacrimation, abdominal cramps, arthralgia, myalgia, vomiting, diarrhea, increased pain.	• *Not in itself* predictive/diagnostic of addiction • Common state with long-term opioid therapy • Treatment not needed for physical dependence • Abstinence requires treatment • Withdrawal may be avoided by tapering opioid therapy
Addiction	Persistent psychological pattern of inappropriate opioid use despite harm to self and others; eg, compulsive preoccupation with obtaining/using opioids, loss of control over opioid use, lack of concern for adverse consequences of opioid misuse.	• Screen patient for risk factors (see Table 4) • Review patient medication history • Document and evaluate aberrant drug-taking behavior (eg, chronic early refills, lost prescriptions, unauthorized dose escalation) • Patients with substance abuse/addiction disorders potentially at higher risk for opioid abuse but can be treated with opioids under controlled circumstances; may require specialty referral • Addiction treatment requires referral to addiction specialist
Pseudoaddiction	Drug-seeking behavior focused on pain relief, due to undertreatment of pain.	• Behavior normalizes with adequate analgesia

Adapted from: *Public Policy Statement on the Rights and Responsibilities of Physicians in the Use of Opioids for the Treatment of Pain*. American Society of Addiction Medicine; 1997.

Use of Opioid Analgesics for the Treatment of Chronic Noncancer Pain–A Consensus Statement and Guidelines. Canadian Pain Society; 1998.

Table 8. Opioid Equianalgesic Conversion (see Table 11 a-c for using ratios)

After optimum titration of dose/frequency, consider changing opioid if:

- Unachieved control of pain
- Unsatisfactory route of administration
- Inadequate onset/duration of action
- Intolerable side effects
- Unacceptable drug-drug interaction
- Dissatisfaction of patient

Step 1 Determine total 24-hour dose of current drug (include controlled-release, immediate release, parenteral). May need to use equianalgesic calculation to convert between routes (use steps 2-3 to combine various routes into one common route and drug for the 24-hour dose).
Example: 30 mg MS Contin q12h + 15 mg MSIR PRN (average use/day = 3 doses)= 60 mg (MS Contin) + 45 mg (MSIR)= 105 mg oral morphine... want to convert this to oxycodone based regimen

Step 2 Locate the equianalgesic dose of the current opioid route and the new opioid route listed in the equianalgesic chart (Table 9a). For fentanyl formulations (except IV) see Table 9c for directions. For methadone, use 24-hour dose (in morphine equivalents) to calculate dose using Table 9b.
Example (cont'd): oral morphine on chart (30) vs oral oxycodone (20) on Table 9a

Step 3 Use a proportion to convert first opioid to new regimen. The answer (X) from the proportion is the total 24-hour dose of the new opioid.

$$\frac{\text{Current total 24-h opioid dose}}{X} = \frac{\text{Equianalgesic dose for current opioid}}{\text{Equianalgesic dose for new opioid}}$$

Example (cont'd): $\frac{105}{X} = \frac{30}{20} \rightarrow \frac{105 \times 20}{30} \rightarrow$ 70 mg PO oxycodone 24-h dose

Step 4 Decide type of regimen is required (long-acting, short-acting, or both) and modify daily dose of new opioid into appropriate time interval using information in Table 9. If long acting agent is q12h, total daily dose would be divided by 2 (# doses/24h). If short-acting agent is to be used q3h, total daily dose should be divided by 8 (# doses/24h). If both are required, structure regimen as with long-acting and calculate rescue doses as described in Table 5.
Example (cont'd): regimen desired is OxyContin (q12h) and OxyIR (q3h) → base on long-acting agent: divide 24-h dose by 2 = 70/2= 35 mg oral oxycodone twice daily. For rescue: 35 x 10-15%= 3.5-5.25 mg oral oxycodone PRN.

Step 5 Assess appropriateness of new regimen and individualize dose. Round to nearest dosage formulation. If pain is controlled when opioids are changed, consider adjusting for incomplete cross-tolerance (decrease calculated dose by 30-50%). Reassess frequently and titrate new drug as described in Table 5.
Example (cont'd): 35 mg rounded to 30 mg Oxycontin and 5 mg OxyIR q3h PRN. (May consider decreasing to 20 mg Oxycontin if concerned with cross-tolerance and pain controlled)

- Formula: Current total 24-hour opioid dose X Equianalgesic conversion factor for new opioid = Dose of the new opioid every 24 hours Equianalgesic conversion factor for current opioid

- Key Considerations

1. All equianalgesic ratios/formulas are approximations; clinical judgment is needed when making dose or drug conversions.
2. If the patient is opioid tolerant and has been taking a high dose of opioid, it is best not to abruptly discontinue the present opioid and convert to the new in one step. This could lead to an overdose, causing undesirable side effects, or an underdose, precipitating severe pain. Instead, in these cases, make the transition starting with 50% of the current opioid dose combined with 50% of the projected dose for the new opioid. Gradual increases in the new opioid drug and decreases in the old can be made until the switch is complete over a period of several days. It may be necessary to adjust the dose of the new opioid (ie, maintain the 50% dose of the old opioid and increase the new opioid for insufficient pain relief). Once the combined doses provide good pain control, drop the old opioid and double the new.

Adapted from: *Pain, 2nd Edition - Clinical Manual*, Margo McCaffery, RN, MS, FAAN: and Chris Pasero, RN, MSNc.

Concomitant Use of Non-opioids

➔ **Use of non-opioids is encouraged to minimize opioid side effects, decrease tachyphylaxis, and lower the total dose of opioid analgesics.**

➔ **Antipyretic/analgesics can be useful both by addressing pain through a different mechanism of action and by reducing fever.**

➔ **Most non-opioids can safely and effectively be combined with opioids and with analgesics in other classes (eg, acetaminophen with ibuprofen with morphine).**

Exceptions:

› There is a risk of Serotonin Syndrome when combining opioids such as meperidine with serotonergic agents.

➔ **Caffeine is thought to be a "potentiator" and some say a co-analgesic, most frequently for migraine headaches.**

Table 9. Non-opioid Drug Regimens

Drug, Brand	Usual Dose*	FDA Indications*	Comments
PARENTERAL			
Ibuprofen *Caldolor®*	400-800 mg iv *q6h*	Mild to moderate pain. Moderate to severe pain as an adjunct to opioid analgesics	See Ketorolac below
Ketorolac *Toradol®*		**Adults:** ≤ 5 days only for moderate-severe pain	Bleeding and ulcers in the stomach and intestine. Contraindications: active peptic ulcer disease, any bleeding risk, advanced renal disease, before surgery, with aspirin or NSAIDs.
TOPICAL			
Diclofenac *Voltaren Gel®*	2g (UE); 4 g (LE) *qid* rubbed into the skin using dosing card Max: 32 g/d total		Wash hands unless they are treated. Avoid bathing for 1 hour. Occasionally causes skin reaction.
ORAL			
Acetaminophen	650-1000 mg *q4-6h*	Pain and fever	Age/weight-related dosing. Rare allergic reactions
Aspirin [OTC] *Bayer®* *Bufferin®* *Ecotrin®*	325 mg 1-2 *q4h* or 3 *q6h* ≤ 12/24 h	Headache, menstrual pain, minor pain of arthritis, muscle pain, pain and fever of colds, toothache	Cardioprotective Bleeding and ulcers in the stomach and intestine. Life-threatening allergic reactions Asthma

Continued on next page.

Table 9. Non-opioid Drug Regimens—*continued*

Drug, Brand	Usual Dose*	FDA Indications*	Comments
NSAIDs – Non-selective			
Diclofenac *Voltaren®*	75 mg *bid*	Arthritis, spondylitis	Heart attack Stroke High blood pressure Heart failure from body swelling (fluid retention) Kidney problems including kidney failure Bleeding and ulcers in the stomach and intestine Low red blood cells (anemia) Life-threatening skin reactions Life-threatening allergic reactions Liver problems including liver failure Asthma attacks in people who have asthma Stomach pain Constipation Diarrhea Gas Heartburn Nausea Vomiting Dizziness
Diflunisal, *Dolobid®*	500 mg *q12h*	Arthritis, mild-moderate pain	
Etodolac *Lodine®*	400 mg *q6-8h* (max: 1200 mg/24h)	Arthritis, acute pain	
Fenoprofen *Nalfon®*	200 mg *q4-6h*	Arthritis, mild-moderate pain	
Flurbiprofen *Ansaid®*	50 mg *qid* 100 mg *tid*	Arthritis	
Ibuprofen [OTC] *Motrin®, Advil®*	400 mg *q6h*	Arthritis, mild-moderate pain, dysmenorrhea	
Indomethacin *Indocin®*	25 mg *tid*	Arthritis, spondylitis, enthesopathies, acute gout	
Ketoprofen *Oruvail®, Orudis®*	75 mg *tid*	Arthritis, pain, dysmenorrhea	
Ketorolac *Toradol®*	10 mg *q4-6h* (max: 40 mg/24h) IV/IM PO	Acute pain	
Mefenamic Acid *Ponstel®*	250 mg *q4h*	Mild-moderate pain, dysmenorrhea	
Meloxicam, *Mobic®*	7.5 mg *qd*	Arthritis	
Nabumetone *Relafen®*	1000 mg *qd*	Arthritis	
Naproxen [OTC] *Aleve®, Naprosyn®, Anaprox®*	250 mg *q6-8h* (max: 1250 mg/24 h)	Arthritis, spondylitis, pain, enthesopathies, dysmenorrhea, acute gout	
Oxaprozin, *Daypro®*	1200 mg *qd*	Arthritis	
Piroxicam, *Feldene®*	20 mg *qd*	Arthritis	
Salsalate *Disalcid®*	1500 mg *bid*; 1000 mg *tid*	Arthritis and related disorders	
Sulindac *Clinoril®*	200 mg *bid*	Arthritis, spondylitis, acute painful shoulder, gouty arthritis	
Tolmetin, *Tolectin®*	400 mg *tid*	Arthritis	
NSAIDs – Selective			
Celecoxib *Celebrex®*			

* See prescribing information for details; Many oral medications contain several ingredients.

Table 10. Opioid Analgesics

Drug	Common Product Names	Starting Dose* (opioid naive)	Notes
Short Acting Agents			
Oxycodone CII	*OxyIR®* and *Roxicodone®* (5 mg, 15 mg, 30 mg) **Oral Solution** (5 mg/5mL: 5 mL and 500 mL) *Oxyfast Concentrated Liquid®* (20 mg/mL; 30 mL) **Combination Products:**	PO: 5-10 mg *q3-4h*** **Note:** (for *Combunox®*) 1 tablet *q6h* PRN. 4 doses maximum per day, maximum duration 7 days	

	APA (mg)	Oxycodone (mg)
Endocet®	325 500 650	5, 7.5, 10 7.5 10
Magnacet®	400	2.5, 5, 7.5, 10
Percocet®	325 500 650	2.5, 5, 7.5, 10 7.5 10
Primalev®	325	2.5, 5, 7.5, 10
Roxicet® (Sol)	325/5 mL	5/5 mL
Roxicet®	325 500	5 5
Roxilox® (Cap)	500	5
Tylox® (Cap)	500	5

With ASA: *Percodan®* (5 mg with 325 mg ASA)
With IBU: *Combunox®* (5 mg with 400 mg IBU)

Long Acting Agents		
	Common Product Names	**Starting Dose* (opioid naive)**
	Oxycontin® (10 mg, 20 mg, 40 mg, 60 mg, 80 mg)	PO: 10-20 mg *q12h*

Short Acting Agents			
Hydromorphone CII	*Dilaudid®* (2 mg, 4 mg, 8 mg) *Dilaudid®* suppository (3 mg) *Dilaudid®* oral liquid (1mg/mL; 480 mL)	PO: 2-6 mg *q3-4h* PRN IV/SQ: 0.5-1.5 mg *q3h* PRN Rectal: 3 mg *q4-8h* PRN	• Caution in severe renal insufficiency (active metabolite may accumulate)

Continued on next page.

Table 10. Opioid Analgesics—*continued*

Drug	Common Product Names	Starting Dose* (opioid naive)	Notes
Short Acting Agents			
Fentanyl CII	*Actiq*® (transmucosal: 200 µg, 400 µg, 600 µg, 800 µg, 1200 µg, 1600 µg) *Fentora*® (buccal: 100 µg, 200 µg, 300 µg, 400 µg, 600 µg, 800 µg)	TM: 200 µg, may repeat dose 15 minutes following completion (max 4 units/day) Buccal: 100 µg may repeat dose 15 minutes following completion IV: 25-100 µg *q2h* PRN	Short-Acting • *Fentora*® for opioid tolerant (≥ 60 mg oral morphine equivalent for > 7 days) • Muscle rigidity may occur with rapid IV administration Long-Acting • Not appropriate for acute pain that is rapidly changing • Do not increase dose < 72 hours after initiation or previous dose change
Long Acting Agents			
	Duragesic® (12 µg/h, 25 µg/h, 50 µg/h, 75 µg/h, 100 µg/h)	TD: 12.5 - 25 µg/h *q72h*	
Short Acting Agents			
Morphine CII	*MSIR*® (10 mg, 15 mg, 30 mg) **Oral Solution** (10 mg/5 mL; 5 mL, 10 mL, 100 mL, 500 mL) *Roxanol*® Concentrated Liquid (20 mg/mL; 30 mL, 120 mL, 240 mL) **Morphine suppository** (5 mg, 10 mg, 20 mg, 30 mg)	PO: 10-30 mg *q3-4h* IV/SQ: 5-10 mg *q 2-4h* Rectal: 10-20 mg *q4h*	• Avoid in severe renal insufficiency (active metabolite may accumulate)
Long Acting Agents			
	Q12H: *MS Contin*®*/Oramorph SR*® (15 mg, 30 mg, 60 mg, 100 mg, 200 mg) **Oral solution** (10 mg/5 mL; 5 mL, 10 mL, 100 mL, 500 mL) **Liquid concentrate** (20 mg/mL; 30 mL, 120 mL, 240 mL) *QDAY:* *Kadian*® (20 mg, 30 mg, 50 mg, 60 mg, 80 mg, 100 mg, 200 mg) *Avinza*® (30 mg, 60 mg, 90 mg, 120 mg)	PO: 15-30 mg *q12h* OR 30-60 mg *q24h*	

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Table 10. Opioid Analgesics—*continued*

Drug	Common Product Names	Starting Dose* (opioid naive)	Notes
Short Acting Agents			
Oxymorphone CII	*Opana*® (5 mg, 10 mg)	PO: 5-10 mg *q4h* IV/SQ: 0.5-1 mg *q3h*	
Long Acting Agents			
	Opana ER® (5 mg, 10 mg, 20 mg, 40 mg)	PO: 5 mg *q12h*	
Short Acting Agents			
Methadone CII	N/A	N/A	• Assess drug interactions carefully • Caution: consulting pain specialist is recommended for dosing and monitoring guidance • May accumulate with repeated dosing, must evaluate 2-5 days after dose adjustment
Long Acting Agents			
	Dolophine/Methadose® (5mg, 10 mg, 40 mg) **Oral solution** (5 mg/5 mL, 10 mg/5 mL; 500 mL) *Methadone Intensol*® concentrated liquid (10 mg/mL; 30 mL)	PO: 2.5-5 mg *q8-12h* IV: 1-2 mg *q8-12h*	
Short Acting Agents			
Tramadol	*Ultram*® (100 mg, 200 mg, 300 mg) Combination product: With APAP: *Ultracet*® (37.5 mg with 325 mg APAP)	PO: 50-100 mg *q4-6h*** Note: maximum dose 400 mg/day (300mg/day if age >75 years)	• Mu agonist and weak inhibitory effect on reuptake of norepinephrine and serotonin • Not a controlled product • May decrease seizure threshold • Avoid in severe renal insufficiency
Long Acting Agents			
	Ultram ER® (100 mg, 200 mg, 300 mg) *Ryzolt*® (100 mg, 200 mg, 300 mg)	PO: 100 mg *qd* Note: maximum dose 300 mg/day	

Continued on next page.

Table 10. Opioid Analgesics—*continued*

Short Acting Agents

Drug	Common Product Names	Starting Dose* (opioid naive)	Notes
Hydrocodone CIII	Combination Products: APA (mg) / Hydrocodone (mg) *Lorcet 10/650®* 650 / 10 *Lorcet®* 650 / 10 *Lorcet Plus®* 650 / 7.5 *Lortab 10/500®* 500 / 10 *Lortab 5/500®* 500 / 5 *Lortab 7.5/500®* 500 / 7.5 *Lortab Elixir®* 500/5 mL / 7.5/15 mL *Lortab®* 500 / 7.5, 10 *Vicodin ES®* 750 / 7.5 *Vicodin HP®* 660 / 10 *Vicodin®* 500 / 5 *Zydone®* 400 / 5, 7.5, 10 With ASA: *Lortab ASA®* (5 mg with 500 mg ASA) With IBU: *Vicoprofen®* (5 mg, 7.5 mg with 200 mg IBU)	PO: 5 mg *q4h* ** Note: (for *Vicoprofen®*) maximum duration 10 days, maximum 5 tablets/day	

Long Acting Agents

Common Product Names	Starting Dose* (opioid naive)
Exalgo®	PO:

Short Acting Agents

Drug	Common Product Names	Starting Dose* (opioid naive)	Notes
Butorphanol CIV	*Stadol®* intranasal (10 mg/mL; 2.5 mL)	IV: 1 mg *q3h* IN: 1 mg (1 spray in one nostril), may repeat in 30-60 min if needed, then repeat *q3-4h*	• Kappa agonist / mu antagonist* • Not ideal agent for long-term use • May precipitate withdrawal symptoms in patients physically dependent on full mu opioids • Analgesia related to these agents is limited by ceiling effect—therefore not recommended for severe or escalating pain

Continued on next page.

Table 10. Opioid Analgesics—*continued*

Short Acting Agents

Drug	Common Product Names	Starting Dose* (opioid naive)	Notes
Tapentadol CII	*Nucynta™* (50, 75, and 100 mg)	PO: 50, 75, and 100 mg	• Mu-opioid-receptor agonist that also inhibits reuptake of norepinephrine. • Most common adverse effects are nausea, dizziness, vomiting, sleepiness, and headaches. • Contraindicated in significant respiratory depression, acute or severe bronchial asthma, or hypercapnia; in patients with paralytic ileus; or in those who are currently using or are within 14 days of using monoamine oxidase inhibitors (MAOIs). • Prescribed "with care" in patients with history of seizure disorder or any condition that would put the patient at risk for seizures. • Potentially life-threatening serotonin syndrome may occur.

NOTE:

* This represents a typical starting dose in an opioid-naive patient. For opioid-tolerant patients, dosing is based on principles of equianalgesic conversions. Titration occurs based on pain response and is typically based on percentage increases in total daily dose. For example, if pain remains uncontrolled: if mild, moderate (25-50% increase in total daily dose); if moderate, severe (50-100% increase in daily dose).

** Note: (for APAP and ASA containing products) maximum 4 g/day of APAP or ASA

- SEE PRODUCT LABELING FOR COMPLETE PRESCRIBING INFORMATION
- CNS depressants can increase an opioid's effect and should be used with caution when added to an opioid regimen
- Substantial interindividual variability exists in patient sensitivity to analgesic effects of opioids
- Geriatric: CNS side effects may be particularly prominent, especially with polypharmacy. Suggest using low end of dosing range and titrating slowly
- IM administration of opioids is not recommended due to painful administration and variable absorption/duration parameters

Table 11a. Equianalgesic Conversion Chart

Drug	PO	IV/SQ
Morphine	30^^	10
Oxycodone	20	N/A
Oxymorphone	10	1
Hydromorphone	7.5	1.5
Fentanyl^^^	N/A	0.1
Tramadol	100^	

Equianalgesic ratios/formulas are for estimating; clinical judgement is needed to decide on actual dose.

^ Not a pure opioid, equianalgesic dose listed is an approximation
^^ May be 60 (instead of 30) in opioid-naive patients with acute pain; use caution
^^^ See Table 9c for conversion information for transdermal, buccal and transmucosal fentanyl

Table 11b. Equianalgesic Conversion to Methadone

Oral morphine equivalent (mg/day) - range for dose to be converted	Ratio of methadone: morphine to be used
< 100 mg	1:3
101 - 300	1:5
301 -600	1:10
601 - 800	1:12
801 - 1000	1:15
< 1000	1:20

Table 11c. Equianalgesic Conversion to Transdermal, Buccal, and Transmucosal Fentanyl

Transdermal	2 mg oral morphine = 1 µg/h TD fentanyl (round to appropriate patch size) 110 mg oral morphine per day = 55 µg/h TD fentanyl → 50 µg/h fentanyl patch 75 µg/h fentanyl patch = 150 mg oral morphine daily →75 mg MS Contin q12h
Transmucosal and buccal	There is no accurate conversion factor for TM fentanyl and other opioids, however there is a correlation available between transmucosal and buccal fentanyl

Actiq Dose Range	Fentora Equivalent
200-400 µg	100 µg
600-800 µg	200 µg
1200-1600 µg	400 µg (200 µg x 2)

Table 12. Risk Management Strategies to Minimize Medication Abuse and Enhance Patient Monitoring

- → **Formal written agreement with patient, after detailed consent discussion, outlining clinician's policy for:**
  - › Providing controlled prescription drug;
  - › Consequences of problematic drug-related behavior;
  - › Criteria for exiting opioid therapy
- → **Obtain all prior health records and permission to contact healthcare providers prior to prescribing**
- → **Prescription of long-acting drug in appropriate quantities for specific duration of time**
- → **Prescription for rescue medication not to exceed more than 2 doses in 24 hours**
- → **Only one specified pharmacy to fill prescriptions, with permission to contact**
- → **No early refills and no replacement of lost prescription without documented/confirmed loss**
- → **Frequent patient appointments, bringing filled prescriptions for unannounced pill counts**
- → **Baseline urine drug screen followed by unannounced future screens**
- → **Require non-opioid therapies as determined, including psychotherapy or referral to addiction medicine specialist if patient at risk or exhibits aberrant behaviors**
- → **Permission for others (eg, spouse, family, friends) to give feedback to physician; consider sincerely expressed concerns**
- → **In states with electronic prescription monitoring/tracking, initial query of database and at regular intervals; respond/follow-up any unsolicited report**

Source: Fine PG, Portenoy RK. *A Clinical Guide to Opioid Analgesia*. New York: MCGraw-Hill Company, Inc.; 2004.

Drug Abbreviations: APAP, acetaminophen (N-acetyl-p-aminophenol); **ASA**, acetylsalicyclic acid; **ATC**, around the clock; **COXIB**, cyclooxygenase selective inhibitor; **IBU**, ibuprofen; **IN**, intranasal; **LE**, lower extremities; **MAOI**, monoamine oxidase inhibitor; **NSAID**, non-steroidal anti-inflammatory drug; **PCA**, patient-controlled analgesia; **SSRI**, selective serotonin reuptake inhibitor; **TD**, transdermal; **TM**, transmucosal; **UE**, upper extremities

Online Resources for Pain Management Information

Alcohol and Drug Abuse Institute Library, University of Washington
http://lib.adai.washington.edu
Agency for Healthcare Research and Quality (AHRQ) http://www.ahrq.gov
American Academy of Pain Medicine http://www.painmed.org
American Pain Foundation http://www.painfoundation.org
American Pain Society http://www.ampainsoc.org
American Society of Addiction Medicine http://www.asam.org/
Chronic Pain Network http://www.chronicpainnetwork.com
Beth Israel-Pain Medicine & Palliative Care http://www.StopPain.org
Drug Enforcement Administration http://www.usdoj.gov/dea
Emerging Solutions in Pain http://www.emergingsolutionsinpain.com/
Federation of State Medical Boards of the United States http:// www.fsmb.org
Institute for Clinical Systems Improvement (ICSI) http://www.icsi.org
International Association for the Study of Pain http://www.iasp-pain.org/
Johns Hopkins-Center for Cancer Pain Research/Pain Site http://www.cancerpain.jhmi.edu/
Joint Commission on Accreditation of Healthcare Organizations (JCAHO)
http://www.jcaho.org/
Mayo Clinic Pain Management Center
http://www.mayoclinic.com/findinformation/diseasesandconditions/index.cfm
MD Anderson Pain Site http://www.mdanderson.org/topics/paincontrol/
MEDLINEplus: Pain http://www.nlm.nih.gov/medlineplus/pain.html
National Foundation for the Treatment of Pain http://www.paincare.org/
National Initiative for Pain Control (NIPC) http://www.painedu.org/nipc.asp
National Pain Education Council http://www.npecweb.org/
National Pain Foundation http://www.NationalPainFoundation.org
Pain.com http://www.pain.com
Pain EDU http://www.painedu.org
Pain and Policy Studies Group http://www.painpolicy.wisc.edu/
Partners Against Pain http://www.partnersagainstpain.com
Practitioners' Manual (2006), Informational Outline of Controlled Substances Act
http://www.deadiversion.usdoj.gov/pubs/manuals/index.html
Substance Abuse and Mental Health Services Administration (SAMHSA)
http://www.kap.samhsa.gov
TALARIA: Hypermedia Assistant for Cancer Pain Management
http://www.painresearch.utah.edu/cancerpain/

Disclaimer

Opioids have been shown to be a proper and effective treatment for selective patient populations with acute, cancer-related, and chronic non-cancer pain. The purpose of this Guideline is to provide information for primary care physicians and other healthcare providers about the current use of opioids in pain management. This Guideline attempts to define principles of practice that should produce high-quality patient care. It focuses on the needs of primary care practice but also is applicable to providers at all levels.
This Guideline should not be considered exclusive of other methods of care reasonably directed at obtaining the same results. The ultimate judgment concerning the propriety of any course of conduct must be made by the clinician after consideration of each individual patient situation.

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